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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/560,595

03/16/2006

Koichiro Kano

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EXAMINER

POPA, ILEANA

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/560,595	Applicant(s) KANO, KOICHIRO	
	Examiner ILEANA POPA	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-34 is/are pending in the application.
- 4a) Of the above claim(s) 20-22,26-28,33 and 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-19,23-25 and 29-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06/25/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/23/2009 has been entered.

Claims 1-14 have been cancelled. Claims 20-22, 26-28, 33, and 34 have been withdrawn. Claim 15 has been amended.

Claims 15-19, 23-25, and 29-32 are under examination.

2. The rejection of claims 15, 18, 23, and 24 under 35 U.S.C. 102(b) as being anticipated by Park et al. (Bone, 1999, 24: 549-554), as evidenced by Lecoœur et al. (Biomaterials, 1997, 18: 989-993, Abstract) is withdrawn in response to Applicant's amendment to the claims field on 06/23/2009.

Information Disclosure Statement

3. The IDS form of 06/25/2009 has been considered. It is noted that the first five non-patent documents have been lined through because Applicant did not provide an English translation of the document, nor did Applicant provide an English abstract.

Art Unit: 1633

Acknowledgment is made of Applicant's submission of an English abstract of the JP2000083656 application.

Applicant is reminded that a proper citation of non-patent documents must include the author name. None of the non-patent document citation includes the author name.

Priority

4. In the non-final Office action mailed on 06/10/2008, the Examiner indicated that, while a certified foreign priority paper has been received, Applicant did not provide an English translation of the foreign priority paper.

As the Examiner stated in the Office action mailed on 12/23/2008 and as Applicant now indicates, since establishing priority will not overcome the art rejections of record, Applicant is not required to submit an English translation of the foreign priority document.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 15-18, 23, 24, 29, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al. (Bone, 1999, 24: 549-554, of record), in view of both

Art Unit: 1633

Lecoeur et al. (Biomaterials, 1997, 18: 989-993, Abstract, of record) and Sugihara et al. (Differentiation, 1986, 31: 42-49, of record).

Park et al. teach isolating, cultivating, and cloning mature adipocytes from human bone marrow; the cloned mature adipocytes are further cultured and dedifferentiated to fibroblast-like fat cells (i.e., pre-adipocytes), wherein the pre-adipocytes do not have lipid droplets and wherein the pre-adipocytes express alkaline phosphatase, i.e., an early marker of osteogenesis (see Lecoeur et al., Abstract) (claim 15); Park et al. teach further transdifferentiating their pre-adipocytes into osteoblasts (claims 18, 23, 24, and 30) (Abstract, p. 550, columns 1 and 2, p. 553, column 1, first full paragraph and column 2). Park et al. teach that obtaining dedifferentiated pre-adipocytes lacking lipid droplets useful to be used in their transdifferentiation method requires continuous trypsinization before the cells reach confluence to inhibit their differentiation by cell-cell contact (p. 550, column 2; p. 551, column 2).

Park et al. do not teach deriving their pre-adipocytes from the dedifferentiation of mature adipocytes isolated from subcutaneous fat tissue, nor do they teach ceiling culture (claims 15 and 17). However, at the time the invention was made, such was taught by the prior art. For example, Sugihara et al. teach a method of obtaining mature unilocular adipocytes from abdominal fat tissue, the method comprising chopping the tissue into small pieces, subjecting the chopped tissue to collagenase digestion followed by filtration and centrifugation, isolating the floating unilocular fat cells, followed by subjecting the isolated unilocular fat cells to "ceiling culture" to obtain fibroblast-like pre-adipocytes (Abstract, p. 42, column 2, p. 44, column 1, second and third paragraphs, p.

Art Unit: 1633

45, column 1, p. 46, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Park et al. by using the ceiling method of Sugihara et al. to achieve the predictable result of obtaining pre-adipocytes suitable to be used in a transdifferentiating method.

Claims 16 and 29 recite that the pre-adipocyte cell line is FERM BP-0864, wherein FERM BP-0864 cell line is obtained by the method of Sugihara et al. (see the instant specification, p. 8, 22, and 23). It is noted that Applicant did not provide any evidence that FERM BP-0864 cell line has unique properties as compared to other cell lines obtained by using a method according to the combined teachings of Park et al. and Sugihara et al. Absent evidence of unexpected results, it is generally not inventive to use the FERM BP-0864 cell line versus similar cell lines obtained by using the same method.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

7. Claims 15-19, 23-25, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al. taken with both Lecoecur et al. and Sugihara et al., in further view of each Ross et al. (Science, 2000, 289: 950-953, of record), Bennett et al. (J Biol Chem, June 7, 2002, 277: 30998-31004, of record), and Rando et al. (J Cell Biol, 1994, 125: 1275-1287, of record).

The teachings of Park et al., Lecoecur et al., and Sugihara et al. are applied as above for claims 15-18, 23, 24, 29, and 30.

Art Unit: 1633

Park et al., Lecoeur et al., and Sugihara et al. do not teach transdifferentiation to myoblasts (claims 19, 25, 31, and 32). However, at the time the invention was made, the prior art suggested that pre-adipocytes have the capability to transdifferentiate into myocytes. For example, Ross et al. teach that adipocytes and myocytes originate from the same precursor and that signaling by Wnt10b is required for commitment to the myocyte lineage; they also teach that inhibition of Wnt10b signaling in pre-adipocytes and myoblasts induces adipogenesis (Abstract, p. 952, columns 2 and 3). Bennett et al. teach that the Wnt10b receptors are highly expressed in pre-adipocytes and that inhibition of Wnt10b signaling leads to adipogenesis (Abstract, p. 30999, column 1, first paragraph). Based on these teachings, one of skill in the art would have known that treating pre-adipocytes with a myoblast differentiation medium comprising Wnt10b would result in their transdifferentiation to myoblasts. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Park et al., Lecoeur et al., and Sugihara et al. by transdifferentiating their pre-adipocytes to myoblasts, with a reasonable expectation of success. The motivation to do so is provided by Rando et al., who teach that myoblasts grown *in vitro* can regenerate muscle fibers when transplanted into a subject in need of treatment (Abstract, p. 1275, column 2, p. 1276, column 1). One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that pre-adipocytes express receptors for factors necessary for myoblast lineage commitment.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant traversed the obviousness-type rejections above on the grounds that the pre-adipocytes of Park et al. are different from those of the claimed invention and that Sugihara et al. do not remedy this deficiency.

Applicant argues that the fibroblast-like adipocytes of Sugihara et al. are obtained by ceiling culture like the present invention. However, Sugihara et al. fails to disclose or suggest obtaining fibroblast-like cells having no lipid droplets, or inducing dedifferentiation by passage culture of the fibroblast-like adipocytes having no lipid droplets. Pre-adipocytes of the present invention are established as pre-adipocyte cell line having no lipid droplets which express an early marker of osteoblast, myoblast or adipocyte during the passage culture. On the other hand, the fibroblast-like adipocytes of Sugihara et al. have lipid droplets, become mature adipocytes by contact inhibition, and synthesize large lipid droplets under the influence of insulin. This is because, unlike the pre-adipocytes of the present invention, the adipocytes of Sugihara et al. are not dedifferentiated (see Tabled 1). Pre-adipocytes of the present invention were obtained in a similar way as disclosed in JP 2000-83656, and have similar characteristics as those of the cells obtained in JP 2000-83656. The position of the Official Action alleges that the cells of Sugihara et al. are presumed to express the same early markers as the pre-adipocytes of the present invention because they are obtained by ceiling culture. However, as shown above, the fibroblast-like adipocytes according to Sugihara et al. retain the characteristics of adipocytes, and it is very unlikely that they express an early marker of osteoblast and myoblast. It is acknowledged that in a stage where a cell is committed to be an adipocyte and

Art Unit: 1633

differentiated, the expression of group of genes which is specific to the differentiation of other cells are suppressed. Though the pre-adipocyte of the present invention is a cell in a stage of pre-adipocyte which has been dedifferentiated from adipocyte, it expresses an early marker of osteoblast and myoblast. The pre-adipocyte of the present invention is very unique and shows unexpected results.

Further, the inventors have confirmed that the adipocyte produced according to the present method does not express Glu4, which is a later and terminal marker of adipocytes (See Evidence 1 and 2 in the appendix). Glu4 has a function of taking glucose into cytoplasm, glucose being a raw material for fat synthesis in response to insulin. Also pre-adipocyte of the present invention is not affected by insulin. This further supports that pre-adipocyte of the present invention is not at the terminal state in the differentiation into an adipocyte, but in the state where it loses functions as an adipocyte and is dedifferentiated.

As mentioned above, pre-adipocytes of the present invention are different from the cells of Park et al. or fibroblast-like adipocytes of Sugihara et al. Even if one were to replace the pre-adipocyte of Park et al. with the cells of Sugihara et al., pre-adipocyte of the present invention could not be obtained.

It would not have been expected that dedifferentiation into osteoblast occurs if Park et al. and Lecoeur et al. are combined. Further the pre-adipocyte of the present invention (FERM BP-0864, claim 14) is not obtained by the method of Sugihara et al., but by dedifferentiation of adipocyte, and has unexpected characteristics. Thus the present invention is unobvious over Sugihara et al.

Art Unit: 1633

As to the specific rejection of claims 15-19, 23-25 and 29-32 over Park et al., Lecoœur et al. and Sugihara et al. in view of Ross et al., Bennett et al., and Rando et al., the Examiner alleges that they disclose that: **(i)** adipocytes and myoblasts originate from pre-adipocytes, **(ii)** pre-adipocyte expresses Wnt10b receptor at high level, and **(iii)** signaling by Wnt10b is required for commitment to the myocyte lineage; the inhibition of Wnt10b signaling in pre-adipocytes and myoblasts induces adipogenesis. The Official Action concludes that one of skill in the art would have known that treating pre-adipocytes with a myoblast differentiation medium comprising Wnt10b would result in their transdifferentiation to myoblasts.

However, Applicant argues, pre-adipocytes of the present invention are different from the cells of either Park et al. or Sugihara et al. and they are not derived from mouse embryo. Wnt10b is not added in inducing differentiation of the pre-adipocytes to myoblasts.

It is well known that it is more difficult to differentiate mesenchymal stem cells into myoblasts than into osteoblasts, adipocytes and chondrocytes, and that there have been few successes in obtaining myoblasts. Even with 10T1/2 cells which are the only mesenchymal stem cells capable of differentiating into skeletal muscle, transcription controlling region of skeletal muscle is highly methylated compared to myoblasts, and the differentiation frequency is very low. Further, C2C12 is the only cell line which can be used for the study of differentiation of skeletal muscle. The only other option to obtain myoblast is to use muscle satellite cells which exist on myofibrils of muscle tissues (See Evidence 3 to 5 of the appendix).

Art Unit: 1633

In view of the above, one of skill in the art would not have expected that myoblasts can be easily obtained from pre-adipocytes of the present invention based on Ross et al. where Wnt10b is used. Ross et al. knocked out Wnt, and used over expression technique to obtain myoblasts from pre-adipocytes. If it were obvious to differentiate pre-adipocytes of the present invention into myoblasts based on the above references alone, as suggested by the Official Action, it would have been obvious to obtain various differentiated cells from ES-cell-like ips cells only because various cells are obtained from ES cells.

In the present invention Wnt10b was not used in differentiation of adipocytes into myoblasts, and specific medium system was found in order to produce skeletal muscle from cells originated from adipocytes.

Therefore, Applicant argues that the present invention is not rendered obvious over cited references and requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, they are not found persuasive for the following reasons:

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). None of the references has to teach each and every claim limitation. If they did, this would have been anticipation and not an obviousness-type rejection. Therefore,

Art Unit: 1633

none the Applicant's arguments individually directed to either Park et al. or Sugihara et al. is found persuasive.

It is the combination of Park et al. and Sugihara et al. which teaches fibroblast-like pre-adipocytes free of lipid droplets obtained by the ceiling culture and using these fibroblast-like pre-adipocytes in a transdifferentiating method.

According to Applicant, the Examiner alleges that the cells of Sugihara et al. are presumed to express the same early markers as the pre-adipocytes of the present invention because they are obtained by ceiling culture. This is incorrect. Park et al. already teach that their pre-adipocytes express the same early markers.

Applicant argues that, even if one were to replace the pre-adipocyte of Park et al. with the cells of Sugihara et al., pre-adipocyte of the present invention could not be obtained. This is just an argument not supported by any evidence, and therefore it is not found persuasive. There is no difference between the ceiling method of Sugihara et al. and the instant ceiling method. Moreover, Park et al. teach how to obtain dedifferentiated fibroblast-like pre-adipocytes lacking lipid droplets useful to be used in their transdifferentiation method. Specifically, they teach that such cells can be obtained by continuous trypsinization before the cells reach confluence to inhibit their differentiation by cell-cell contact (p. 550, column 2; p. 551, column 2). Applicant did nothing more. Therefore, one of skill in the art would have known to apply the teachings of Park et al. to the method of Sugihara et al. such as to obtain dedifferentiated fibroblast-like pre-adipocytes lacking suitable for transdifferentiation. Clearly, the cells

Art Unit: 1633

taught by the combination of Park et al. and Sugihara et al. are not different from the instant cells.

And even assuming, for the sake of the argument, that the cells of Park et al. and Sugihara et al. would be different from the instant cells, there is no evidence of record that using the instant cells as opposed to the cells taught by Park et al. and Sugihara et al. results in differentiated cells with superior properties. Using the instant pre-adipocyte is not significant if it does not provide a novel feature over using the pre-adipocyte taught by the prior art.

Applicant argues that it would not have been expected that dedifferentiation into osteoblast occurs if Park et al. and Lecoeur et al. are combined. It is not clear why Applicant is making this argument. As indicated in the rejection above, Park et al. already teach transdifferentiation to osteoblasts. Lecoeur et al. was only used to evidence that, similar to the instant cells, the pre-adipocytes of Park et al. express early markers of osteogenesis.

Applicant argues that the pre-adipocyte cell line FERM BP-0864 is not obtained by the method of Sugihara et al. and has unexpected characteristics. This argument is not found persuasive because there is no evidence of record that the FERM BP-0864 cell line has unique properties as compared to other cell lines obtained by using a method according to the combined teachings of Park et al. and Sugihara et al. An argument does not replace evidence.

Applicant states that one of skill in the art would not have expected that myoblasts can be easily obtained from pre-adipocytes. None of the Applicant's evidence and arguments to support this statement is found persuasive.

For example, Applicant argues that Wnt10b is not added in inducing differentiation of the pre-adipocytes to myoblasts. This is not found persuasive because the claims do not exclude using Wnt10b. The claims recite "inducing transdifferentiation of preadipocyte cell line". Such a broad recitation clearly does not exclude the use of Wnt10b to induce transdifferentiation to myoblasts.

Applicant argues that is well known that it is more difficult to differentiate mesenchymal stem cells into myoblasts than into osteoblasts, adipocytes and chondrocytes, and that there have been few successes in obtaining myoblasts. This argument is irrelevant to the instant rejection which is drawn to differentiating pre-adipocytes and not mesenchymal stem cells into myoblasts. None of the evidence provided by Applicant proves that one of skill in the art would not have reasonably expected to be successful in differentiating pre-adipocytes to myoblasts.

Applicant argues that, if it were obvious to differentiate pre-adipocytes of the present invention into myoblasts based on the above references alone, as suggested by the Official Action, it would have been obvious to obtain various differentiated cells from ES-cell-like ips cells only because various cells are obtained from ES cells. This argument is again irrelevant to the instant rejection.

For the reasons set forth above, the claimed invention is rendered *prima facie* obvious by the combination of art cited above.

Art Unit: 1633

8. Claims 15-18, 23, 24, 29, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al., in view of both Lecoœur et al. and Kano et al. (JP2000-083656, Abstract, Applicant's IDS).

Park et al. teach isolating, cultivating, and cloning mature adipocytes from human bone marrow; the cloned mature adipocytes are further cultured and dedifferentiated to fibroblast-like fat cells (i.e., pre-adipocytes), wherein the pre-adipocytes do not have lipid droplets and wherein the pre-adipocytes express alkaline phosphatase, i.e., an early marker of osteogenesis (see Lecoœur et al., Abstract) (claim 15); Park et al. teach further transdifferentiating their pre-adipocytes into osteoblasts (claims 18, 23, 24, and 30) (Abstract, p. 550, columns 1 and 2, p. 553, column 1, first full paragraph and column 2). Park et al. teach that obtaining dedifferentiated pre-adipocytes lacking lipid droplets useful to be used in their transdifferentiation method requires continuous trypsinization before the cells reach confluence to inhibit their differentiation by cell-cell contact (p. 550, column 2; p. 551, column 2).

Park et al. do not teach deriving their pre-adipocytes from the dedifferentiation of mature adipocytes isolated from subcutaneous fat tissue, nor do they teach ceiling culture (claims 15 and 17). However, at the time the invention was made, such was taught by Kano et al. It is noted that, although the Applicant only submitted an English language abstract, in his remarks filed on 06/23/2009, Applicant admits that the pre-adipocytes of the present invention are obtained in a similar way as disclosed in JP 2000-083656, and have similar characteristics as those of the cells obtained in JP 2000-083656. Therefore, Kano et al. teach a ceiling method of preparing pre-adipocytes, the

Art Unit: 1633

method comprising obtaining mature unilocular adipocytes from abdominal fat tissue and dedifferentiating these unilocular adipocytes to pre-adipocytes having no lipid droplets and expressing an early marker of osteoblast, myoblast, or adipocyte, as recited in claim 15. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Park et al. by using the ceiling method of Kano et al. to achieve the predictable result of obtaining pre-adipocytes suitable to be used in a transdifferentiating method.

Claims 16 and 29 recite that the preadipocyte cell line is FERM BP-0864. As admitted by the Applicant, the FERM BP-0864 cell line is obtained by the method of Kano et al. It is noted that Applicant did not provide any evidence that FERM BP-0864 cell line has unique properties as compared to other cell lines obtained by using a method according to the combined teachings of Park et al. and Kano et al. Absent evidence of unexpected results, it is generally not inventive to use the FERM BP-0864 cell line versus similar cell lines obtained by using the same method.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

9. Claims 15-19, 23-25, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al. taken with both Lecoeur et al. and Kano et al., in further view of each Ross et al., Bennett et al., and Rando et al.

The teachings of Park et al., Lecoeur et al., and Kano et al. are applied as above for claims 15-18, 23, 24, 29, and 30.

Art Unit: 1633

Park et al., Lecoeur et al., and Kano et al. do not teach transdifferentiation to myoblasts (claims 19, 25, 31, and 32). However, at the time the invention was made, the prior art suggested that pre-adipocytes have the capability to transdifferentiate into myocytes. For example, Ross et al. teach that adipocytes and myocytes originate from the same precursor and that signaling by Wnt10b is required for commitment to the myocyte lineage; they also teach that inhibition of Wnt10b signaling in pre-adipocytes and myoblasts induces adipogenesis (Abstract, p. 952, columns 2 and 3). Bennett et al. teach that the Wnt10b receptors are highly expressed in pre-adipocytes and that inhibition of Wnt10b signaling leads to adipogenesis (Abstract, p. 30999, column 1, first paragraph). Based on these teachings, one of skill in the art would have known that treating pre-adipocytes with a myoblast differentiation medium comprising Wnt10b would result in their transdifferentiation to myoblasts. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Park et al., Lecoeur et al., and Kano et al. by transdifferentiating their pre-adipocytes to myoblasts, with a reasonable expectation of success. The motivation to do so is provided by Rando et al., who teach that myoblasts grown *in vitro* can regenerate muscle fibers when transplanted into a subject in need of treatment (Abstract, p. 1275, column 2, p. 1276, column 1). One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that pre-adipocytes express receptors for factors necessary for myoblast lineage commitment.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Art Unit: 1633

10. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Weitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633

Application/Control Number: 10/560,595
Art Unit: 1633

Page 18